

## PARALDEHYDE

### Use

Paraldehyde can be used to achieve the rapid short term control of persistent non-hypoglycaemic convulsions resistant to a full loading dose of IV phenobarbital (q.v.). An intranasal dose of lorazepam (q.v.) seems just as effective in children, and is easier to give in an out-of-hospital setting, but such an approach has not yet been tested in the neonate.

### Pharmacology

Paraldehyde, a polymer of acetaldehyde, has been used for a century as a sedative-hypnotic and for seizure control. It is a potent anticonvulsant capable of controlling seizures refractory to phenobarbital and phenytoin without causing respiratory depression. It exerts its action rapidly and is then eliminated from the body with a half-life that which is rather variable, but only a little shorter than that of most other anticonvulsants used in the neonatal period. It crosses the placenta, but there is nothing to suggest that its use is hazardous in pregnancy. There are no reports of use during lactation.

Drug elimination is by oxidation to acetaldehyde and carbon dioxide in the liver and also by direct excretion through the lungs. Dispersal into body tissues is very variable ( $V_D \sim 4$  l/kg). The half-life in babies is also very variable (8–27 hours) but generally rather longer than in children (7½ hours) and adults (6 hours). The dose given does not need to be modified in babies with kidney failure because renal clearance is negligible, but the drug's variable and prolonged half-life makes repeated dosing unwise in the first few weeks of life. It has been suggested that high barbiturate levels can retard drug clearance by the liver, probably because of competition for the liver's oxidative pathways, but this remains to be confirmed. It is equally possible that the prolonged half-life often seen in the first week of life could be a consequence of the impact of intrapartum asphyxia on liver metabolism. The management of babies in whom EEG evidence of seizure activity persists despite treatment with both phenobarbital and phenytoin (q.v.) is in urgent need of further study. Paraldehyde has fallen out of favour, but might well turn out to be quite effective if a blood level of 100 mg/l can be achieved. Clonazepam (q.v.) lidocaine (q.v.) and valproate (q.v.) are alternatives currently under study.

The IM route was once widely used in babies, but standard texts now generally consider the rectal route safer. Large IM injections are certainly painful, and they can cause an unpleasant sterile abscess with subsequent muscle and/or nerve damage, but such problems are very uncommon following the deep intramuscular injection of volumes not exceeding 1ml (which is all that any neonate should need), and the response to an IM injection is much quicker than the response to rectal administration. Rectal diazepam was once widely used to control seizures in a home setting, but it is more effective, and much more acceptable, to give a dose of liquid lorazepam or midazolam (q.v.) into the nose or mouth. Indeed, this approach provides an extremely effective way of controlling prolonged seizure activity in *any* setting when IV access proves difficult.

### Treatment

**Rectal:** Give a single 0.4 ml/kg dose of paraldehyde mixed with an equal volume of olive oil (or mineral oil).

**Intramuscular:** Give 0.2 ml/kg *deep* IM. A second identical dose can be given if seizures persist or recur, but no further doses should be given for 48 hours after that because of the drug's unpredictable half-life.

**Intravenous:** Paraldehyde *can* be given as an IV infusion, but the use of this route is now generally discouraged, and it is not really necessary given the drug's long neonatal half-life. To give 0.4 ml/kg of paraldehyde (the maximum safe dose) as an IV infusion, dilute 2.5 ml of paraldehyde to 50 ml with 5% dextrose and then give 4 ml/kg of this solution over *just two hours* as a slow continuous infusion.

### Supply and administration

**Supply:** Amber glass bottles which contain 15 ml of paraldehyde already mixed with 15 ml of olive oil are available on special order in the UK for rectal administration. They cost £6. Ampoules of pure paraldehyde (containing 1 g/ml) are still available in some countries, but are no longer marketed in the UK. Never use either product if there is brown discolouration, or if there is a sharp pungent odour of acetic acid when the container is first opened. Keep all products below 25°C during storage.

**Administration:** Paraldehyde reacts chemically with rubber and with most plastics (polythene and polypropylene syringes being more resistant than those made of polyvinyl chloride [PVC]), but it can be given using any plastic syringe as long as it is injected just as soon as it is drawn up. However a polypropylene syringe (such as a Plastipak® syringe made by Becton Dickinson), and a polypropylene extension set (such as one of the products marketed by Vygon) **must** be used if a sustained IV infusion is to be given.

### References

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